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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/457,771 12/09/99 EMANUELE R 19720-0624

HM22/0607

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EXAMINER

SCHNIZER, R

ART UNIT	PAPER NUMBER
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1632

DATE MAILED:

06/07/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/457,771

Applicant(s)

Emanuelle et al

Examiner

Richard Schnlzer

Group Art Unit

1632

☐ Responsive to communication(s) filed on _____☒ This action is **FINAL**.☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 1-16 is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.☒ Claim(s) 1-16 is/are rejected.☐ Claim(s) _____ is/are objected to.☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.☐ The drawing(s) filed on _____ is/are objected to by the Examiner.☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.☐ The specification is objected to by the Examiner.☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been received.☐ received in Application No. (Series Code/Serial Number) _____☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 4☐ Interview Summary, PTO-413☐ Notice of Draftsperson's Patent Drawing Review, PTO-948☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

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DETAILED ACTION

This application is a continuation of 09/104088, abandoned 4/11/00. The claims introduce no new matter, and are substantially the same as those previously rejected in the office actions of 9/10/99, 8/7/95, 4/1/96, 3/5/97, and 12/24/97.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78).

Appropriate correction is required.

Claim Objections

Claims 6 and 7 are objected to because of the following informalities: As written they are dependent upon each other, claim 6 depends on claim 7, and claim 7 depends on claim 6.

Appropriate correction is required.

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Claim Rejections - 35 USC § 112

Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph for the reasons of record set forth in the Office Action of 8/7/95, and as further discussed in the Office Actions of 4/1/96, 3/5/97, and 12/24/97, as containing subject matter which was not described in the specification in such a way as to enable one of skill in the art to make and/or use the invention.

Applicant's claims are broadly directed to methods and compositions for delivering genes or gene products into the body for therapeutic purposes which are not enabled by the specification in view of the highly unpredictable and complex nature of the subject matter. The claimed invention broadly encompasses the transfer of all types of nucleic acids (e.g. genes oligonucleotides, RNA) into any and all cell types, tissues, and animals, including humans, such that one of skill in the art would be unable to practice the invention without undue experimentation, or with a reasonable expectation of success.

Factors to be considered in the determination of enablement include the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, and the breadth of the claims. Considerations for any gene therapy protocol include, for example, the choice of target gene and tissue, dosage and route of administration, the efficiency of gene transfer the level and duration of gene expression or inhibition necessary to exert a therapeutic effect, the action of complement and the immune system, as well as nucleases and proteases in the circulation, and safety issues including

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the toxicity of the delivery system and possible oncogenic transformation. Applicant has claimed a broad range of block copolymer compositions but has not supplied sufficient guidance for one of skill in the art to choose a specific copolymer composition, in terms of the molecular weight of the polyoxypropylene (POP) component, the percentage weight of polyoxyethylene (POE), or the amount of surfactant or alcohol included. It is not made clear if the choice of these parameters is critical to the success and predictability of the invention, or if all of the copolymers in the claimed range will produce therapeutic benefit in vivo. Applicant has provided no justification for the assertion that “ the copolymers most effective as therapeutic agents are high molecular weight and have low percentages of POE - generally less than 20% POE (page 17), especially in light of the absence of working examples of in vivo therapeutic application. Five of the copolymer compositions are tested for their effect on in vitro transfection of COS cells in Example IX. One of the copolymers tested, CRL 1187, has the lowest molecular weight in the group (750) and the highest percentage weight of POE (25%) - yet, at 5% transduction, performed the best of the five. Two of the copolymers, CRL-1183 and CRL-8131, performed no better than standard dextran/glycerol transfection(2%). The 2.5-fold difference in efficiency between two copolymer compositions within the range of the claimed invention attests to the unpredictability of using the invention. There is insufficient evidence that a sufficient number of target cells could be transduced in vivo by the claimed invention to exert a therapeutic effect. In the absence of working examples, the applicant has not enabled methods of therapeutic delivery of the nucleic acid to humans or animals as broadly encompassed in the claims.

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Applicant has not responded to the Office Action of 9/10/99.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5, 8, and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "nucleic acid sequence" of claims 5, 8, and 16 is indefinite because it is unclear exactly what is to be delivered with the copolymer.

The phrase "capable of expressing" in claims 8 and 16 is open to interpretation and renders the claims indefinite as to their metes and bounds.

Applicant has not responded to the Office Action of 9/10/99.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simons et al (1992) Nature 359:67-70; Hunter, U.S. 5,030,4⁴88; and Allison et al, U.S. 4,772,466 for the reasons of record set forth in the Office Action of 8/7/95, and as further discussed in the office actions of 4/1/96, 3/5397, and 12/24/97.

Hunter describes a method of delivering drugs to diseased or damaged tissue using an ethylene oxide - propylene oxide copolymer. In claim 14 of the Hunter reference, the drug is identified as from a group consisting of antibiotics, antifungal drugs and chemotherapeutic drugs, anti-inflammatory drugs, and anticoagulants, among others. Hunter does not specifically disclose the delivery of nucleic acids with the claimed invention. The block copolymer of the Hunter invention has a POP molecular weight range from 950 to 4000, and a POE percent weight range from 50-90%. Simons describes the delivery of antisense c-myc oligonucleotides to rat arterial smooth muscle cells by the application of a composition of antisense oligonucleotide and Pluronic (TM) gel, for the purpose of inhibiting gene expression and cell proliferation. Simons used Pluronic (TM) F-127, which has a POP molecular weight of about 4000, and is 70% POE by weight. Neither Simons nor Hunter discloses the same POP molecular weight range or percent weight range of POE claimed by applicant. Allison discloses the use of POP-POE block copolymers to deliver antigen in vivo for the purpose of vaccination. The POP component of Allison has a molecular weight range of 2000-15,000 (page 3, lines 52-59) and a 1-30% weight of POE (page 4, lines 17-28). A surfactant, preferably Tween(TM) 20, is included in an amount of 0.5-2.5%, "to stabilize the emulsion or suspension formed" (see pages 4 and 5). While not

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specifically disclosed in the references, minor components might be added that do not essentially affect the performance of the invention, such as alcohol which is a well-known preservative and solubility enhancer. Though there is a small difference between the preferred ranges of Allison and those of applicant, Allison discloses the desirability of a high molecular weight POP component and a low percentage weight of POE, just as applicant discloses in the specification (page 18, lines 19-24). Thus, Allison and Hunter in combination disclose the POP molecular weight range and the percent POE range claimed by applicant. Both Hunter and Allison provide the motivation to use block copolymers with a POP molecular weight range of 950-15,000, and a POE percent weight of 1-90%. Thus it would have been obvious to one of ordinary skill in the art at the time the invention was made to specifically deliver nucleic acids with a POP-POE copolymer as taught by Simons, and to use a POP-POE copolymer within the specific POP molecular weight and POE percent weight ranges described by Hunter and Allison to deliver a variety of pharmaceutical products with increased therapeutic efficacy.

Applicant has not responded to the Office Action of 9/10/99.

Conclusion

No claim is allowed.

This is a continuation of applicant's earlier Application No. 09/104088, Which was a continuation of applicant's earlier Application No. 8/926,297, which was a continuation of applicant's earlier Application No. 08/725,842. All claims are drawn to the same invention

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claimed in the earlier applications and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly,

THIS ACTION IS MADE FINAL even though it is a first action in this case. See MPEP

§ 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37

CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 703-306-5441. The examiner can normally be reached on Mondays and Thursdays between the hours of 6:20 AM and 3:50 PM, and on Tuesdays, Wednesdays and Fridays between the hours of 7:00 AM and 4:30 PM (Eastern time). The examiner is off every other Friday, but is usually in the office anyway.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jasmine Chambers, can be reached at 703-308-2035. The FAX phone number for art unit 1632 is 703-308-0294.

Inquiries of a general nature or relating to the status of the application should be directed to the group receptionist whose telephone number is 703-308-0196.

Richard Schnizer, Ph. D.


BRUCE R. CAMPPELL
PRIMARY EXAMINER
GROUP 1800